REMARKS

Claims 10-26 are pending. Claims 10, 15, 17, 20, and 22 have been amended, and claims 27 and 28 have been added.

Claim 10 has been amended as follows. The phrases "inflammation or pain" (three occurrences) and "inflamed or painful joint" (1 occurrence) have been amended to read "inflammation and pain" and "inflamed and painful joint," respectively. The phrase "administration of an effective amount of pantothenic acid or a derivative thereof" has been amended to read "...administration of a composition consisting essentially of an effective amount of pantothenic acid or a derivative thereof and a solvent therefor." Support for these amendments can be found throughout the Specification, e.g., at page 1, lines 26-28; and page 2, at lines 12-15; and in claims 1-4 as originally filed.

Applicants have inserted the phrase "a separate injection of" into claims 15, 17, 20, and 22 following the recitation of "co-administered with." Applicants have also added new claim 27. Support for these amendments and for new claim 27 can be found throughout the Specification. For example, the Specification teaches:

> According to the present invention there is provided use of pantothenic acid or a derivative thereof in the preparation of a medicament for administration by injection into the region of a joint for alleviation of inflammation or pain (Specification, at page 1, lines 17-19).
>
> The initial treatment may cause some pain and it may, therefore, be desirable to co-administer a local anesthetic, e.g. lignocaine, at the same time or shortly before the injection of the pantothenic acid. Other physiologically active materials may be co-administered, e.g. cysteine or glucosamine (Specification, at page 1, line 28 through page 2, line 4).

The sole route of administration taught by the Specification is local injection at the inflamed and painful joint, and co-administration of an additional agent can be coincident or noncoincident

with the administration of the pantothenic acid medicament injection. Therefore, co-administration of an additional agent, e.g., an anesthetic; cysteine or glucosamine; or surface-active phospholipid, corresponds to a local injection of the additional agent that is either separate from or inclusive with the pantothenic acid medicament injection.

The phrase "joint lubricant" has been inserted into claims 17 and 22 following the recitation of "active phospholipid." Support for these amendments can be found throughout the Specification, e.g., page 2, lines 5-11.

Support for new claim 28 can be found throughout the Specification, e.g., at page 2, line 19.

No new matter has been introduced by these amendments. The amendments are made in order to expedite prosecution of this application and entry is respectfully requested as they raise no new issues that will require further consideration or search and also do not touch the merits of the application within the meaning 37 C.F.R. §1.116(b).

Claims 10-15 and 20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hyodo, et al., U.S. Patent 5,260,289 (Hyodo). According to the Examiner:

> ... Hyodo does teach an injectable composition and method of using the same, which comprises calcium pantothenate. ... Moreover, the instantly claimed methods do not preclude additional 'active ingredients' from being administered with calcium pantothenate. ... claim 10, the only independent claim in the instant application, and the only claim that claims a method of alleviating inflammation, is written in the alternative (Office Action, page 3, lines 1-2, 5-7, and 12-14).

Hyodo discloses and claims a method for alleviating pain that includes "injecting a composition containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid" (Hyodo, col. 2, lines 18-21). The subjects being treated by the claimed method are administered with a composition containing the antiphlogistic steroid and "Neo Vitacain," (Hyodo, col. 3, lines 19-21 and col. 5, line 50 through col. 7, line 6). According to Hyodo, Neo Vitacain is a known analgesic having a formulation containing "dibucaine

hydrochloride, sodium salicylate, and calcium bromide as 'active ingredients' for use in a pain treatment," along with "thiamine HCl," "pyridoxin HCl," and "calcium pantothenate" (Hyodo, col. 1, lines 28-49, emphasis added). Since calcium pantothenante is not listed among the "active ingredients" in Neo Vitacain, Hyodo provides no basis to conclude that calcium pantothenate possesses analgesic properties or would be an active agent for the treatment of pain. Moreover, there is no indication in Hyodo that calcium pantothenate is useful for treating inflammation.

Claim 10 as amended is directed to methods for alleviating inflammation and pain in an inflamed and painful joint of a mammal. Claim 10 therefore no longer refers to either pair of conjunct terms in the alternative. The method includes locally administering (i.e., injecting) an effective amount of a pantothenic acid medicament into the inflamed and painful joint of the mammal. To clarify the nature of the administered medicament, Applicants have amended claim 10 to recite "...administration of a composition consisting essentially of an effective amount of pantothenic acid of a derivative thereof and a solvent therefor..." The "consisting essentially of" language limits the claim to the specified materials (i.e., pantothenic acid or a derivative thereof) and "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention (i.e., alleviating inflammation and pain in an inflamed and painful joint). *In re Herz*, 537 F.2d 549, 551-552, 190 USPQ 461, 463 (CCPA 1976 emphasis in original).

Hyodo discloses treating pain only by administering a formulation containing "dibucaine hydrochloride, sodium salicylate, and calcium bromide as 'active ingredients' for use in a pain treatment," along with "thiamine HCl," "pyridoxin HCl," and "calcium pantothenate." Hyodo does not disclose administration of calcium pantothenate as the single and exclusive active ingredient for treating pain and inflammation as is required by claim 10 as amended. Hyodo therefore does not anticipate claim 10 as amended. Since claims 11-15 and 20 depend from claim 10, then Hyodo does not anticipate these dependent claims either. Applicants respectfully request withdrawal of the rejection and that the rejection not be applied to new claims 27 and 28.

Rejections under 35 U.S.C. 103(a)

Claims 10-16 and 20-21 remain rejected as being unpatentable over Hyodo, as applied to claims 10-15 and 20 above and further in view of UK Patent Number 1,145,623 (the '623 Patent). According to the Examiner:

> ... Hyodo teaches a method of using a composition comprising NEO VITICAN™, which comprises 110-mg/100ml of calcium pantothenate and 110-mg/100ml of dibucaine hydrochloride (a local anesthetic), for the local treatment of pain. However, the primary reference lacks the cysteine or glucosamine of instant claim 16 or 21. ... The 623 reference teaches a composition comprising d-pantothenic acid and cysteine for parenteral administration (Office Action, page 7, lines 20-23 and page 8, lines 11-12).

The '623 Patent discloses compositions containing *d*-pantothenic acid, or physiologically acceptable salts thereof, and cysteine or cystine. These compositions are described to be useful for the alleviation of arthritis. According to the '623 Patent specification, the compositions may be adapted for oral, parenteral or rectal administration ('623 Patent, page 1, lines 74 and 82 and page 2, line 18). In other words, the '623 Patent teaches only systemic treatment of arthritis using the combination of d-pantothenic acid (or salts thereof) and cysteine or cystine. Moreover, only oral administration is exemplified.

As discussed elsewhere, calcium pantothenate is disclosed essentially by happenstance in Hyodo, as merely being part of the Neo Vitacain formulation. There is no teaching or suggestion in Hyodo that calcium pantothenate plays any role in the treatment of pain, regardless of whether Neo Vitacain is administered alone or in combination with the antiphlogistic steroids. Further there is no teaching in Hyodo that would motivate one of skill in the art to select calcium pantothenate from the list of formulation ingredients (Hyodo, col. 1, lines 40-50 and col. 5, lines 23-43) and test it for effectiveness in pain treatment by local administration. Again, Hyodo discloses compositions that require dibucaine hydrochloride, sodium salicylate and calcium bromide, administered along with an antiphlogistic steroid. It would therefore not have been obvious to one of ordinary skill to try to treat pain by local administration of calcium

pantothenate in the absence of Neo Vitacain and the antiphlogistic steroid on the basis of the Hyodo disclosure.

Claim 10 as amended is directed to methods for alleviating inflammation and pain in an inflamed and painful joint of a mammal. The method includes locally administering (i.e., injecting) an effective amount of a composition consisting essentially of pantothenic acid or a derivative thereof and a solvent therefor into the inflamed and painful joint of the mammal. Dependent claims 15 and 20 as amended are directed to methods that further include co-administration of an anesthetic by separate injection. Dependent claim 16 and new claim 28 are directed to methods that further include co-administration of cysteine or glucosamine.

As discussed elsewhere, one of ordinary skill in the art would not have been motivated to select the satellite ingredient, calcium pantothenate, from Hyodo and formulate it with any therapeutic agent, let alone an anesthetic or cysteine or glucosamine.

First, the Specification teaches that an anesthetic may be administered to alleviate the pain associated with the initial treatment with the pantothenic acid. Further, the anesthetic may be administered shortly before the pantothenic acid administration, i.e., as a separate injection. This limitation is neither taught nor suggested by Hyodo.

Second, Hyodo teaches local administration of compositions containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid to treat pain. One of skill in the art would not have been motivated to (1) select the satellite ingredient, calcium pantothenate, from the local pain treatment formulation of Hyodo, and (2) modify the local method of Hyodo to include the systemic compositions of the '623 Patent because the compositions demonstrated to have pain relief activity in Hyodo (i.e., the composition containing dibucaine, a pharmaceutically acceptable salt of salicylic acid, calcium bromide, and antiphlogistic steroid) are distinct and different (structurally, functionally, and local v. systemic) from those compounds demonstrated to have pain relief activity in the '623 Patent (i.e., d-pantothenic acid or physiologically acceptable salts and cysteine or cystine). Furthermore, neither Hyodo nor the '623 Patent discuss treatment of inflammation.

Applicants submit that Office has failed to establish a *prima facie* case on the grounds that there would be no motivation to modify Hyodo or combine it with the '623 Patent to arrive at Applicants' claimed invention. Applicants respectfully request that the rejection be withdrawn and not be applied to new claims 27 and 28.

Claims 10-24 remain rejected and claims 25 and 26 are newly rejected as being unpatentable over Hyodo et al. taken with UK Patent Number 1,145,623, as applied to claims 10-16 and 20-21 and further in view of Rozenburg, RU 2078564C1 (Abstract only; Rozenburg).

Rozenburg discloses "Aseptic inflammations can be treated more effectively by administering glucocorticoids...by administering them in a liposome membrane. The liposomal composition...consists of (wt.%): dipalmitoyl phosphatidylcholine [DPPC] (1.6-2.0); cholesterol (0.20-0.25)" (Rozenburg). Rozenburg discloses that DPPC is a useful adjunct for improving the effectiveness of glucocorticoids in the treatment of septic inflammations *vis a vis* as a liposomic carrier for the active component used in Rozenburg. On the other hand, the Specification states "surface active phospholipid (SAPL) such as dipalmitoyl phosphatidylcholine (DPPC)...are believed to act as a lubricant in joints, taking over to some extent the function of sinovial fluid" (Specification, page 2, lines 9 and 13-14).

Claim 10 as amended is directed to methods for alleviating inflammation and pain in an inflamed and painful joint of a mammal. The method includes <u>locally</u> administering (i.e., injecting) an effective amount of a composition consisting essentially of pantothenic acid or a derivative thereof and a solvent therefor into the inflamed and painful joint of the mammal. Dependent claims 17 and 22 as amended are directed to methods that further include co-administration of surface-active phospholipid <u>by separate injection</u> to serve as a joint lubricant.

Rozenburg discloses that DPPC can be useful as liposomic carriers for active ingredients useful in treating inflammation. Rozenburg also discloses that DPPC is administered together with the active ingredients, presumably to maximize contact with the active ingredients and carrier. However, claims 17 and 22 as amended require that the surface-active phospholipids be administered separately. Applicants submit that Rozenburg teaches away from the modification needed to arrive at Applicants' claimed methods. Therefore, one of ordinary skill in the art

would not be motivated to combine the teachings of Rozenburg, with those of the '623 Patent and Hyodo to arrive at Applicants' claimed method.

Applicants submit that all claims are in condition for allowance.

Enclosed is a $475 check for the Three Month Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 13596-003US1.

Respectfully submitted,

Date: August 17, 2004

John T. Kendall, Ph.D.
Reg. No. 50,680

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

20915098.doc